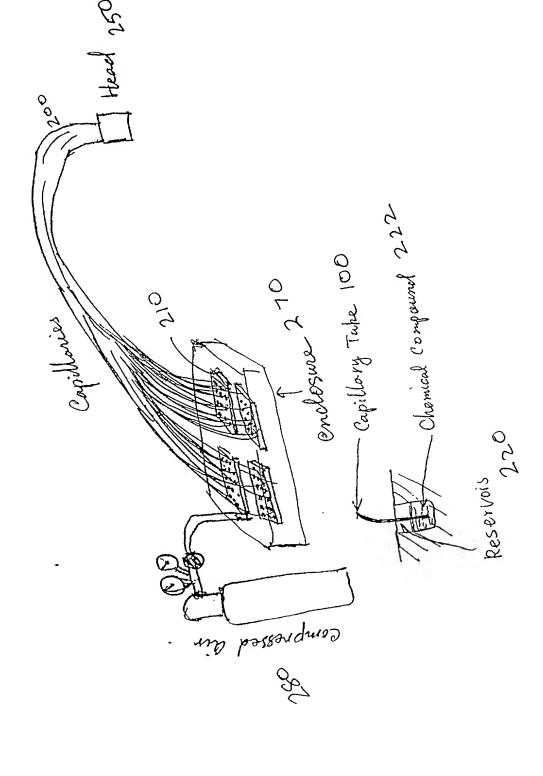


FOR HIGH THROUGHPUT SCREENING
THE: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES

F19. 2A

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097 Imaging Pressure chamber Compound library in microtiter plates 270 -- Microarrays and Fiber Bundles XHTS FlG. 2B assay 230 9 200 222 220 220

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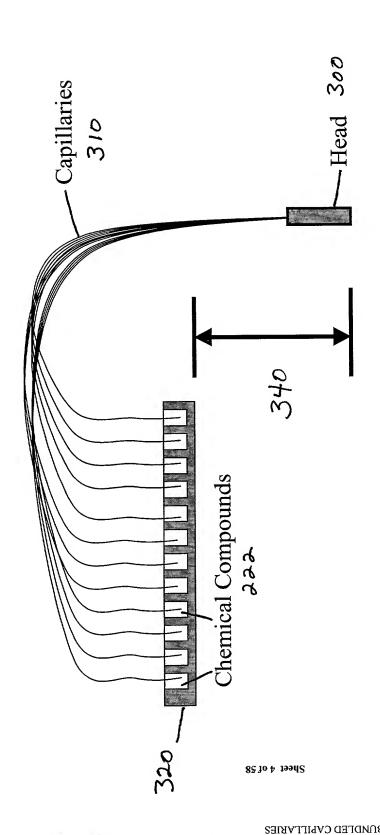


Figure 3

Title: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES FOR HIGH THROUGHPUT SCREENING Inventor: Jiannning XIAO et al. Application No.: To Be Assigned Docket No.: 473532000620

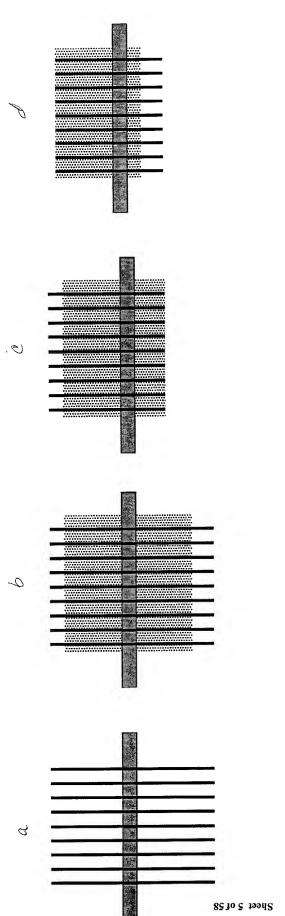
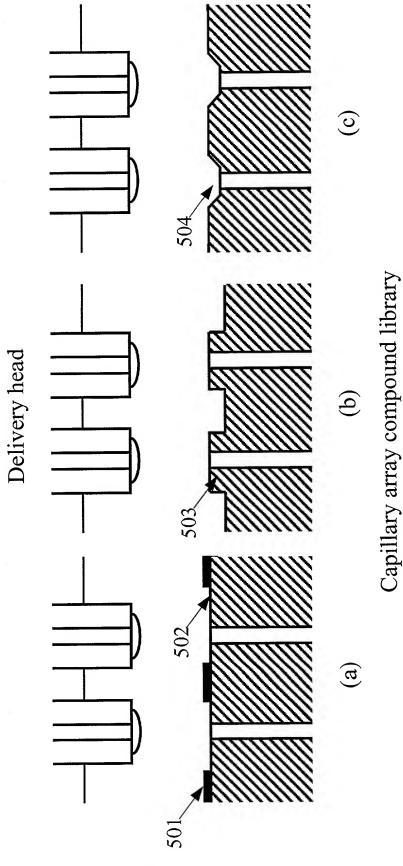


Fig. 4. Fabrication of delivery head using a guide plate

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501 – Hydrophobic coating 502 – Hydrophilic coating 503 – Island

Fig. 5. Surface features on the surface of the capillary array compound library to prevent crosscontamination during compound loading

504 - Well

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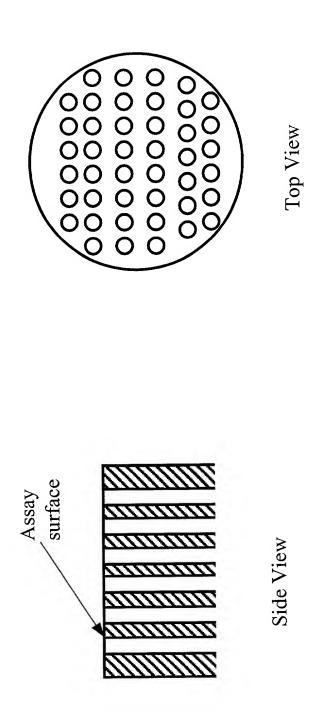


Fig. 6. Basic configuration of capillary array substrate for the portable compound library

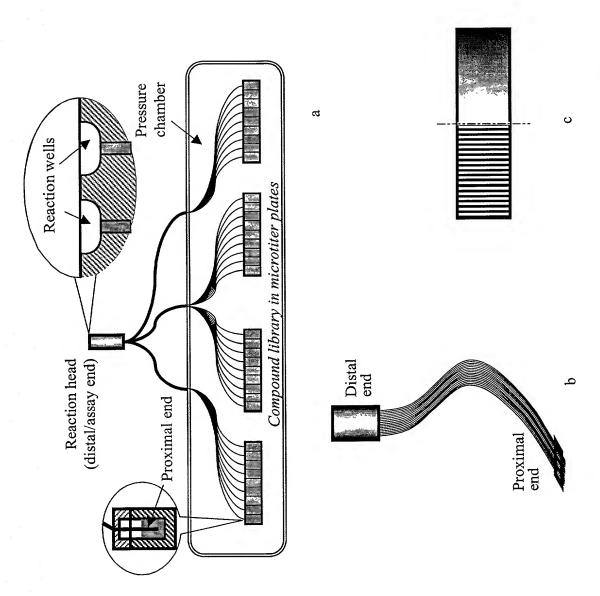
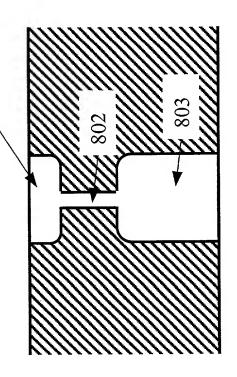


Fig. 7 The capillary array compound library in different formats

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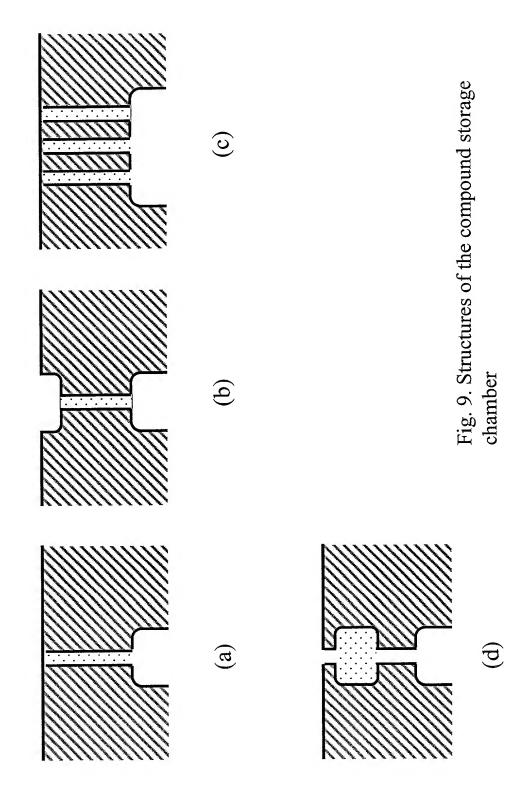
Title: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES
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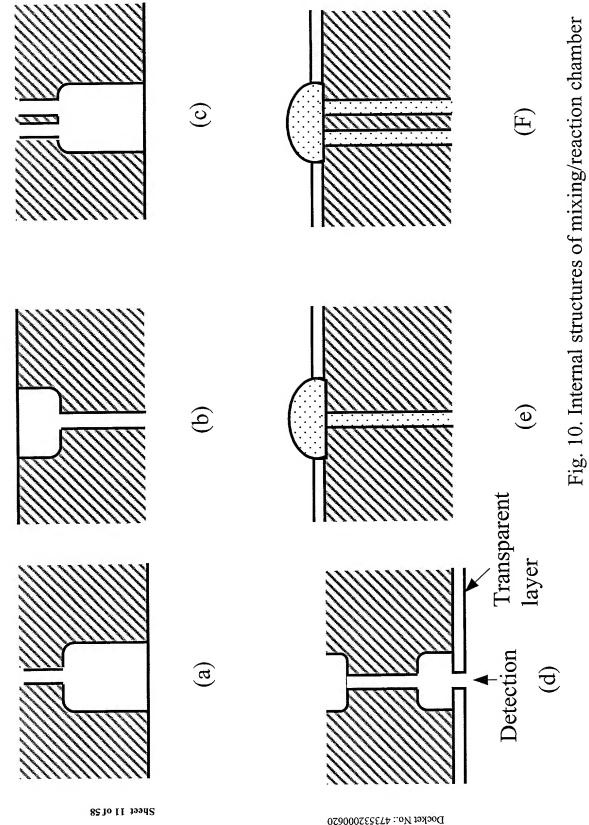
802 - Flow regulator for reagent metering 801 - Mixing/reaction well 803 - Compound reservoir

Fig. 8. Internal structure of a through hole in capillary array compound library

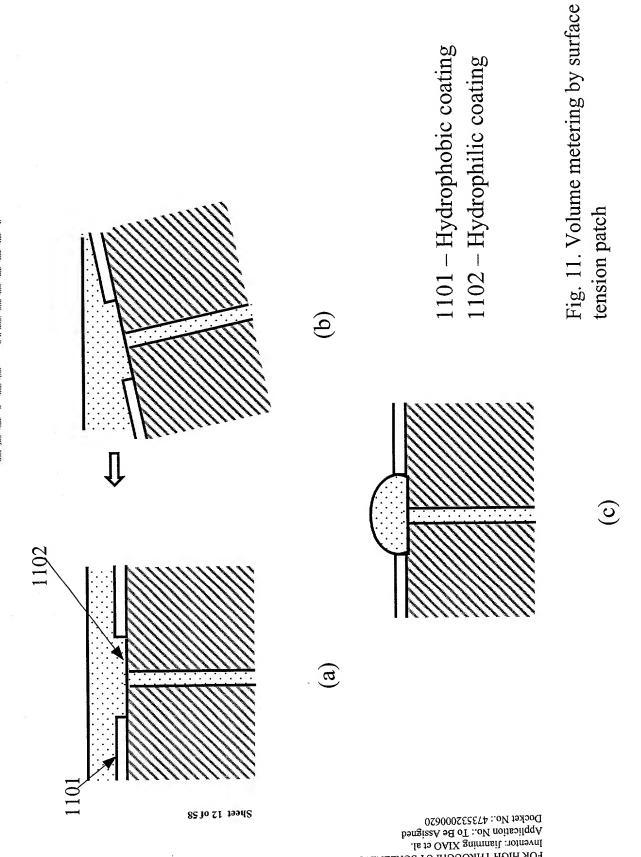


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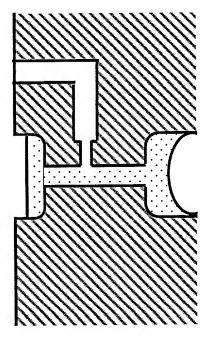
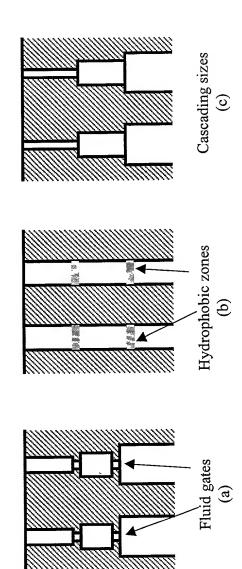


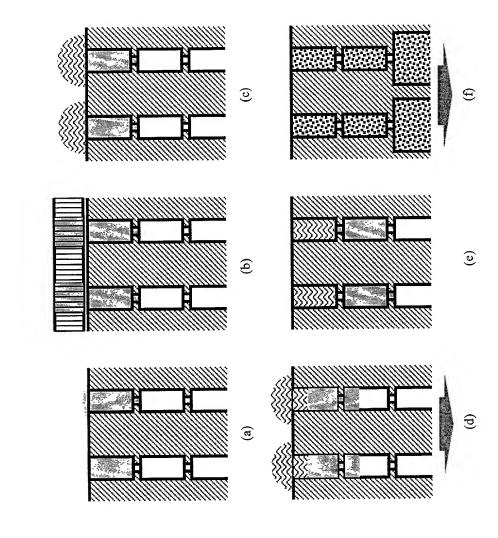
Fig. 12. Fluid regulator with side air tunnel

Fig. 13 Internal through hole structures to facilitate chamber volume metering and mixing



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Fig. 14 Process of metering multiple reagents using interconnected chambers



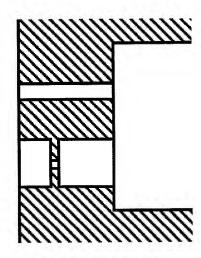
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Fig. 15 Special through hole structure where multiple chambers links to a chamber in parallel



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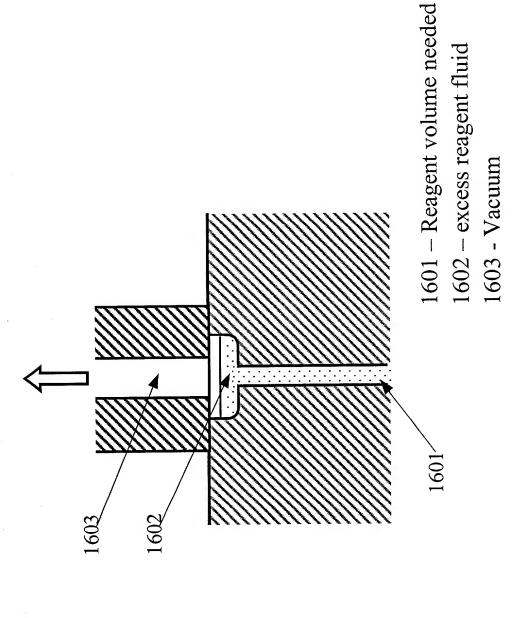


Fig.16. Removal of excess fluid by vacuum

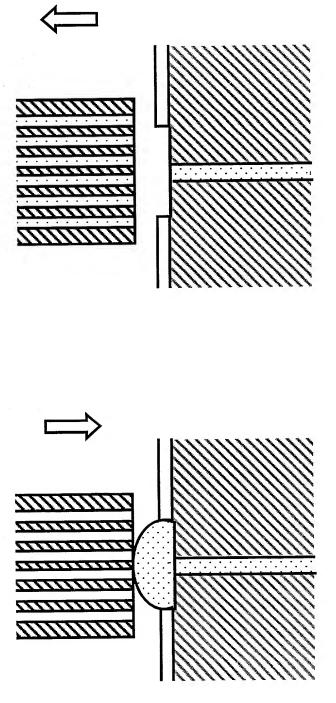
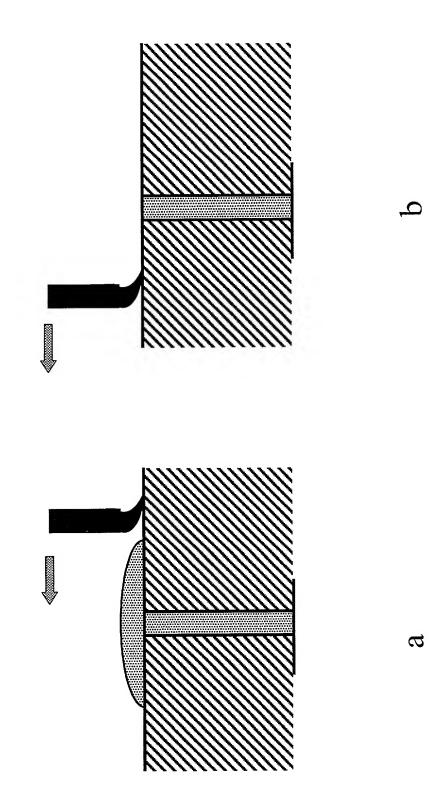


Fig. 17. Excess fluid removal using a second capillary array

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Fig. 18. Excess Fluid Removal by Wiping



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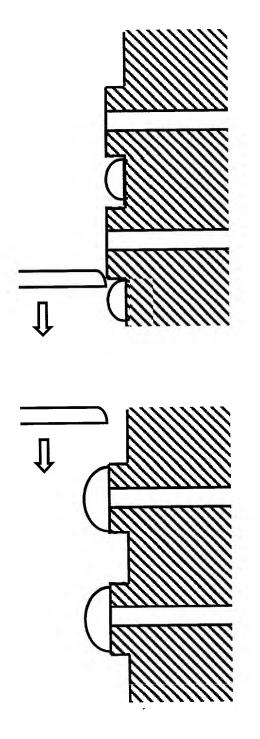
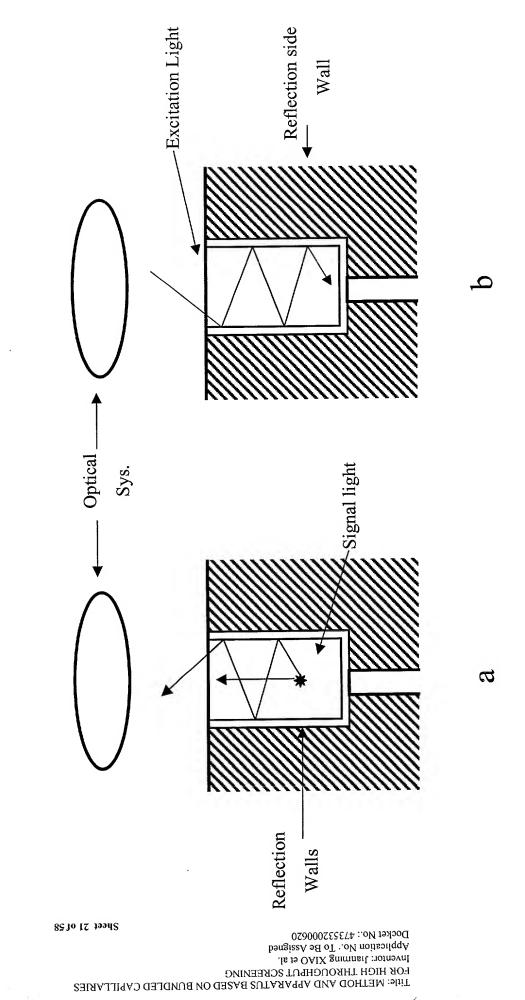
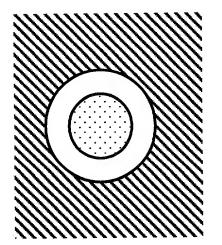


Fig.19. A method for reducing cross-contamination between adjacent holes during excess fluid removal

Fig. 20 Use Reflection Wall of Reaction Chamber to Enhance Optical Signal of the Assay





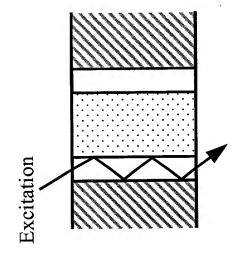


Fig21 Light guiding capillary

1. Immobilization on glass

2. Deprotection (by TFA)

O-Si In

O-Si

n=0, 1, 8 R=-OH₃-C₂H₃-C₂H₄-

FIG. 22A

Si N Soligo

Blocking Step:

other blocking options to be tested:

HS

FIG 22B

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FIG. 22C

Process for Tabrication using a negative mask Figure 23

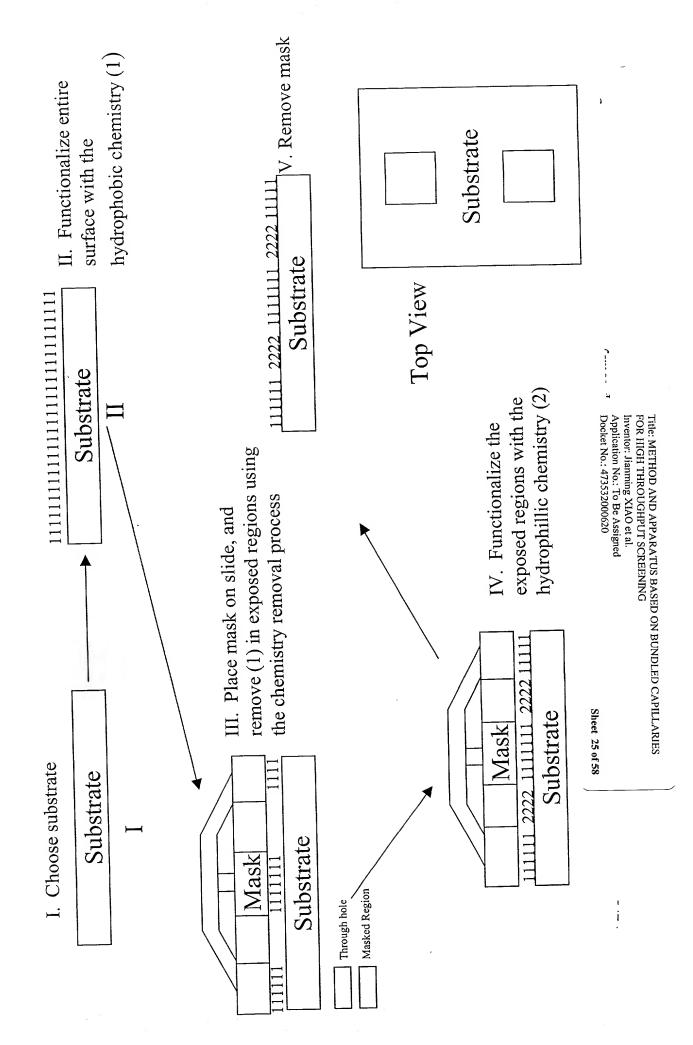


Figure 24 Process for the fabrication using positive mask

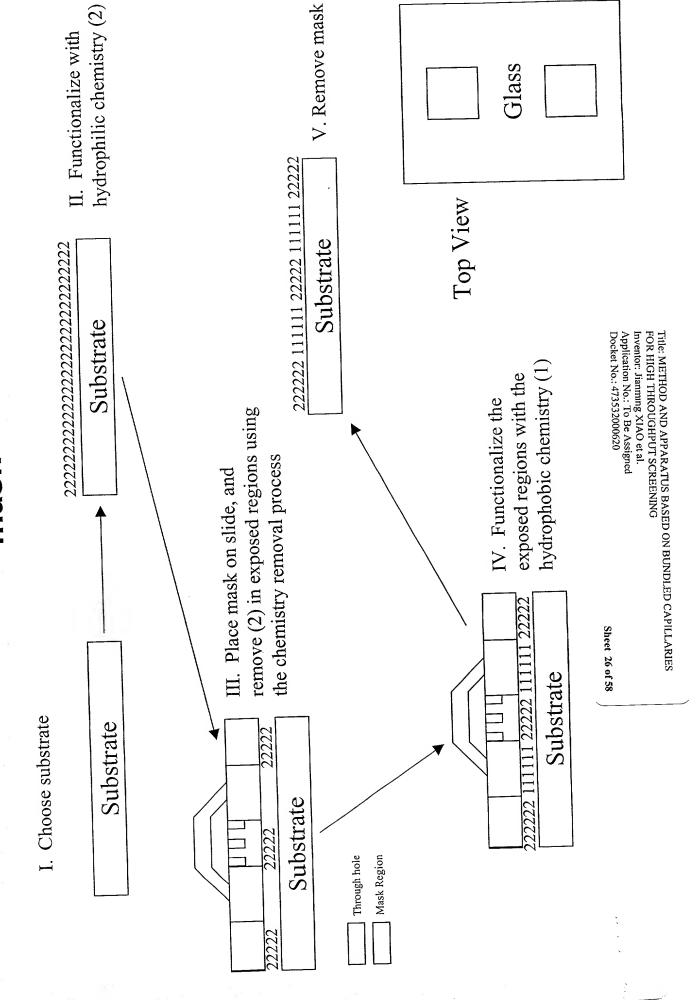


Figure 25 Chamber use

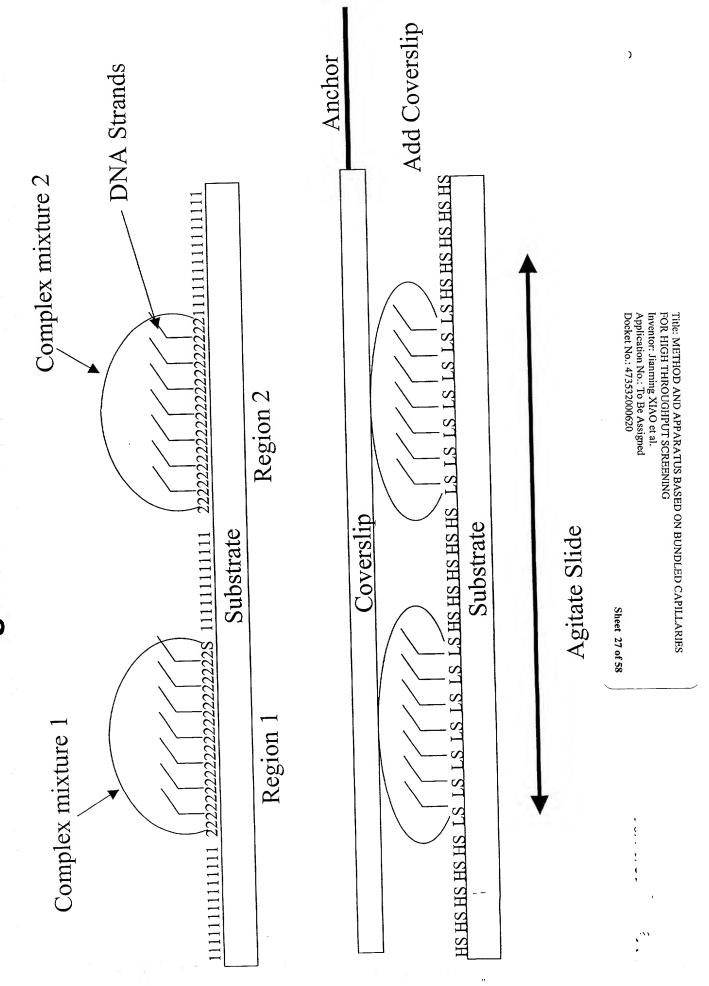
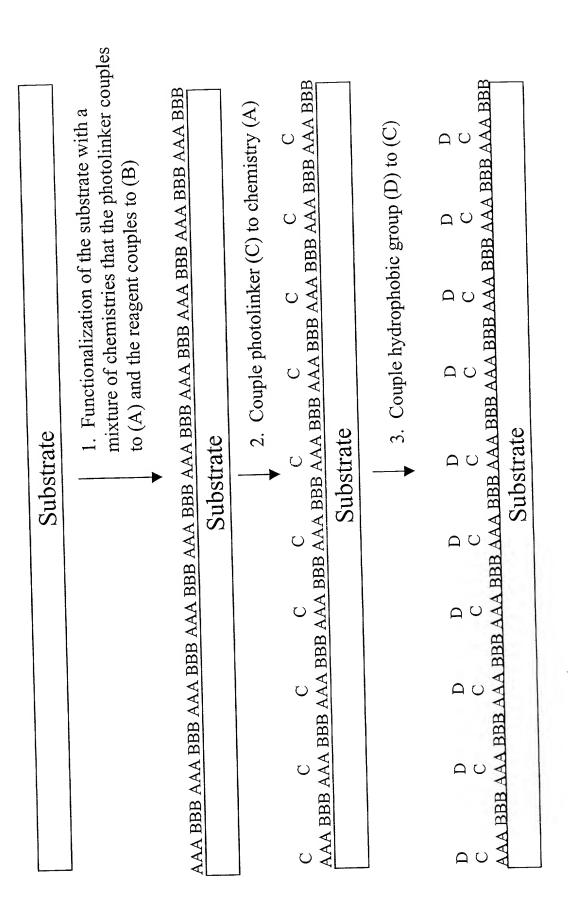


Figure 26A Surface Tension Patterning: On-capillary Fiber optic based patterning



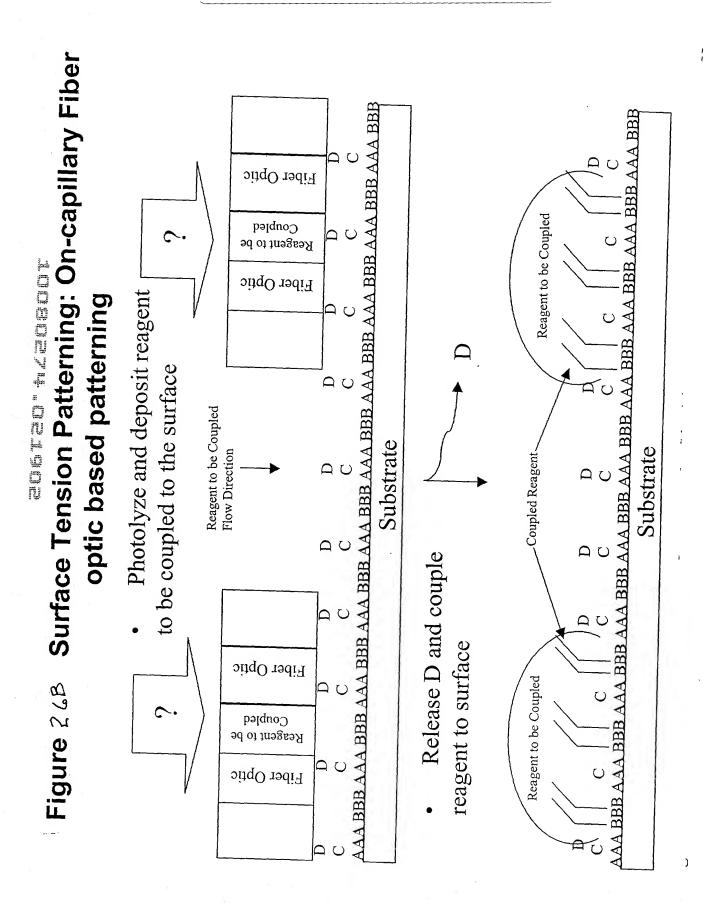
FOR HIGH THROUGHPUT SCREENING inventor: Jianming XIAO et al.

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Glass
Fiber Optic

Glass

Glass

Fiber Optic

Fiber Optic Glass Glass Fiber Optic

Fiber Optic

Glass

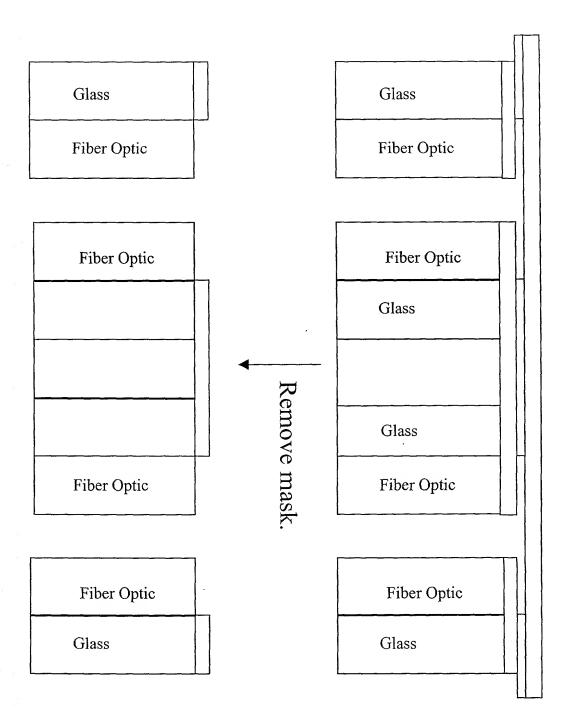
Glass

Fiber Optic

Fiber Optic
Glass

Coat Surface with a Hydrophobic Reagent

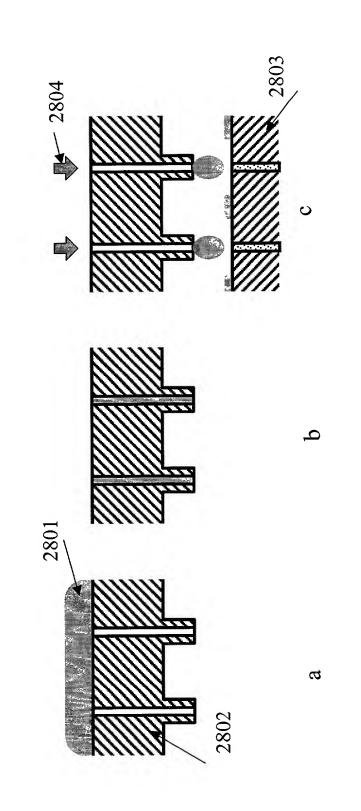
Volume Metering using Surface Tension Features



Place a Mask on to the Surface and Expose the Surface to the Chemistry Removal Process

Figure 278 Volume Metering using Surface Tension Features

Fig. 28 Reagent pre-metering using an intermediary through-hole array



2801 - reagent fluid applied in excessive; 2802 - intermediary through hole array;

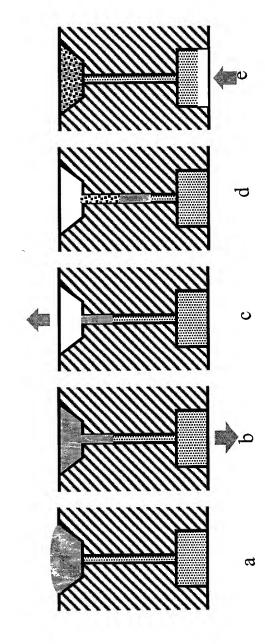
2803 - capillary array compound library;

2804 - pressure

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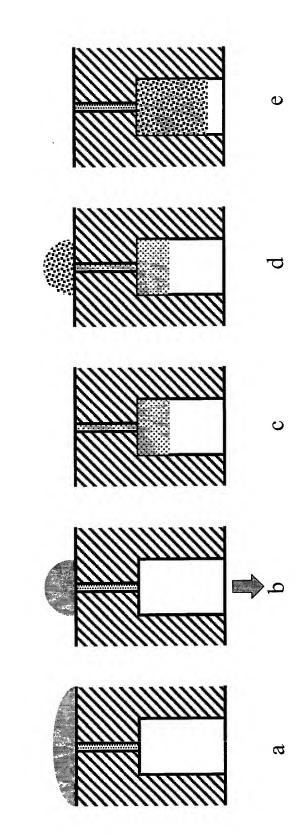
Fig. 29 Metering and mixing with a multi-use capillary array compound library



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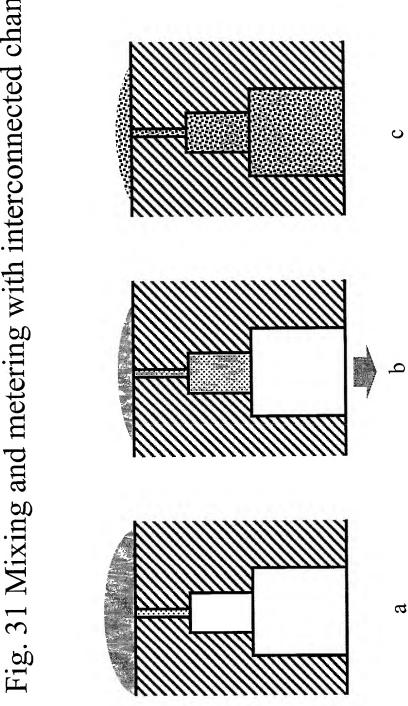
Fig. 30 Metering with hydrophilic patch and mixing



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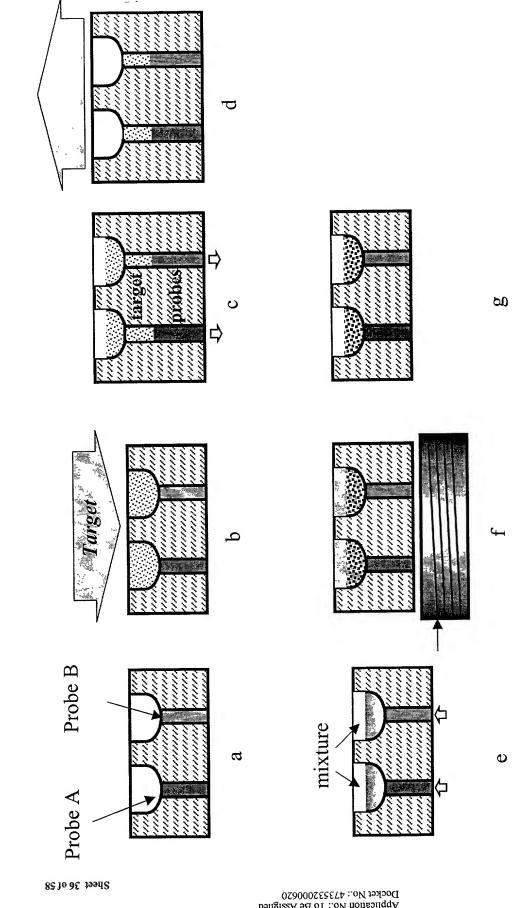
Fig. 31 Mixing and metering with interconnected chambers



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Fig. 32 Heterogeneous Assay



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Antibody Immobilization via the Carbohydrate Moiety

. Oxidation of antibodies vicinal diol group to its aldehyde

2. Conjugation of maleimide moiety with antibody

3. Immobilization of the modified antibody to the surface.

F1G. 33/

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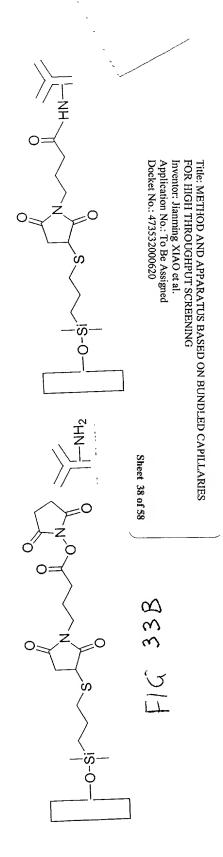
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Immobilization via Amine Goups

1. Hydrosilylation of (3-mercaptopropyl)triethoxysilane on the surface of fiber

2. Formation of a thioether bond

3. Attachment of fiber to antibody



Antibody Immobilization via Streptavidin

1. Label antibody with biotin

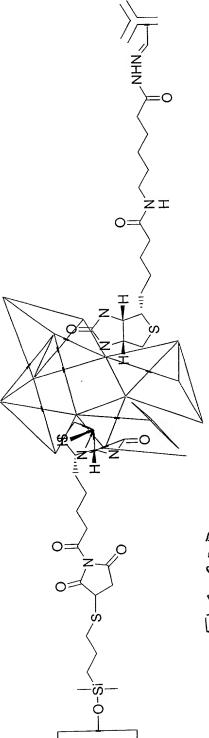
2. Modification of fiber surface with biotin maleimide

FIG 33C

Antibody Immobilization via **Streptavidin**

3. Conjugate Streptavidin to the surface

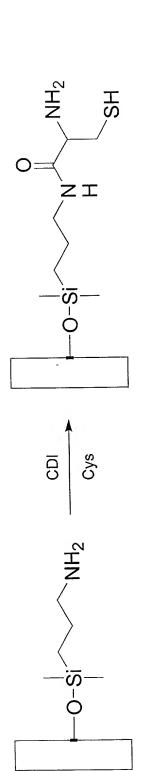
4. Conjugate Biotin Anitbody to the surface



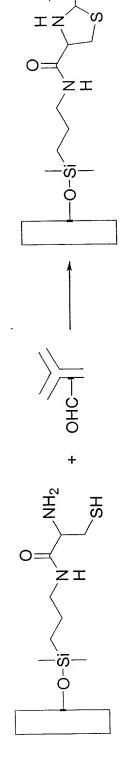
F16.33D

Formation of

. Surface attachment and formation of the linker



Thiazolidine formation رن آ



33 E

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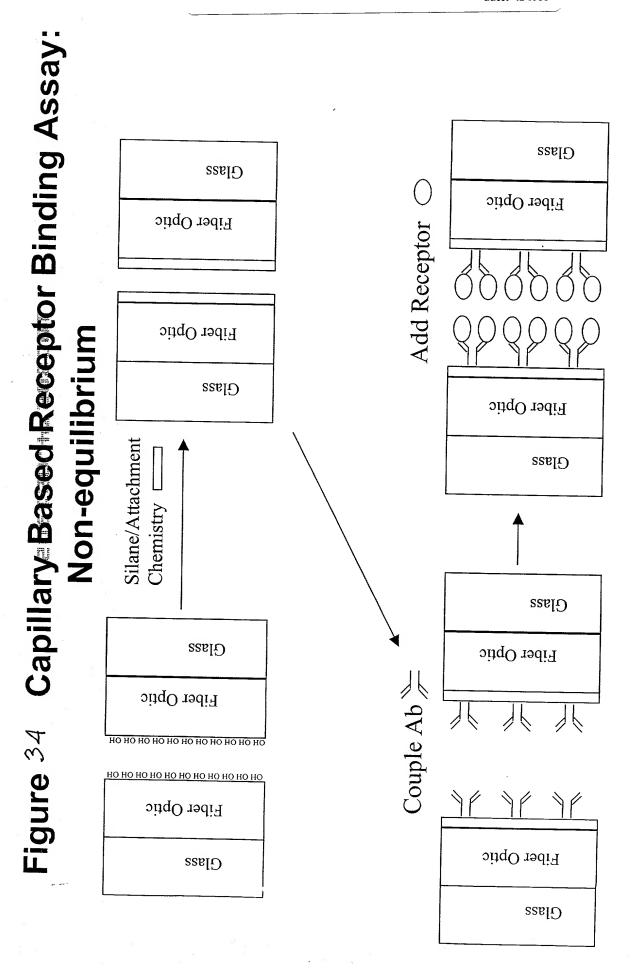
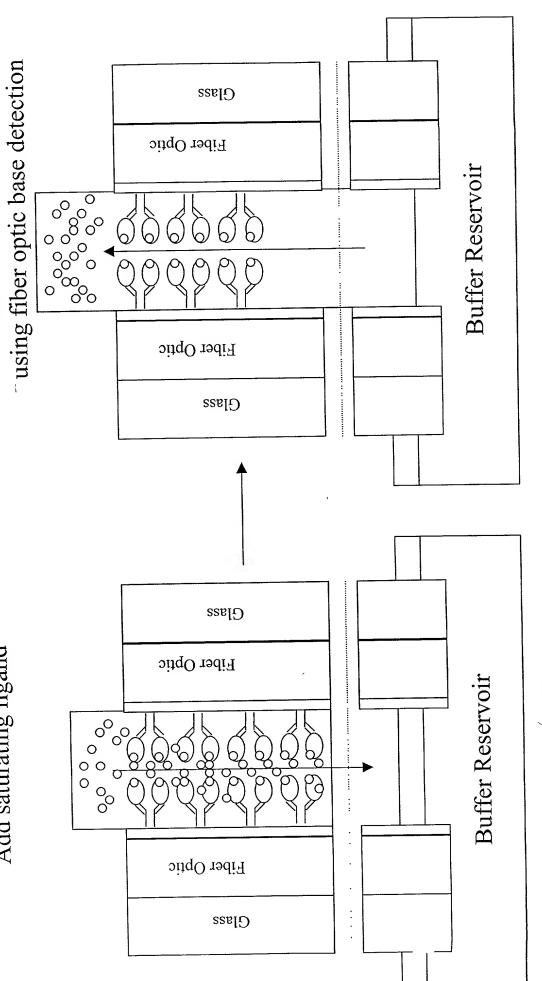


Figure 34 (cont. 1). Capillary Based Receptor Binding Wash unbound ligand Assay: Non-equilibrium

Add saturating ligand

and calculate total bound



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Figure 34 (cont. 2). Capillary Based Receptor Binding Assay: Non-equilibrium

Add compound and use fiber optic based detection to observe kinetics

. 0 8 0 0 0 0 0 Glass 0 0 0 Reservoir Fiber Optic --00000 00000 0 0 0 0 O kinetics Fiber Optic 0 0 Inventor: Jianming XIAO et al.
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Docket No.: 473532000620 Title: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES FOR HIGH THROUGHPUT SCREENING 0 Glass 0 00 0 Second Reservor Glass Fiber Optic compound reservoir Sheet 44 of 58 Move capillary to 000000 Fiber Optic 0 ∞ Glass ∞ 8 O 0 0

igure 34 (cont. 3). Capillary Based Receptor Binding

Assay: Non-equilibrium

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Mover capillary to buffer reservoir and wash

Dry capillary

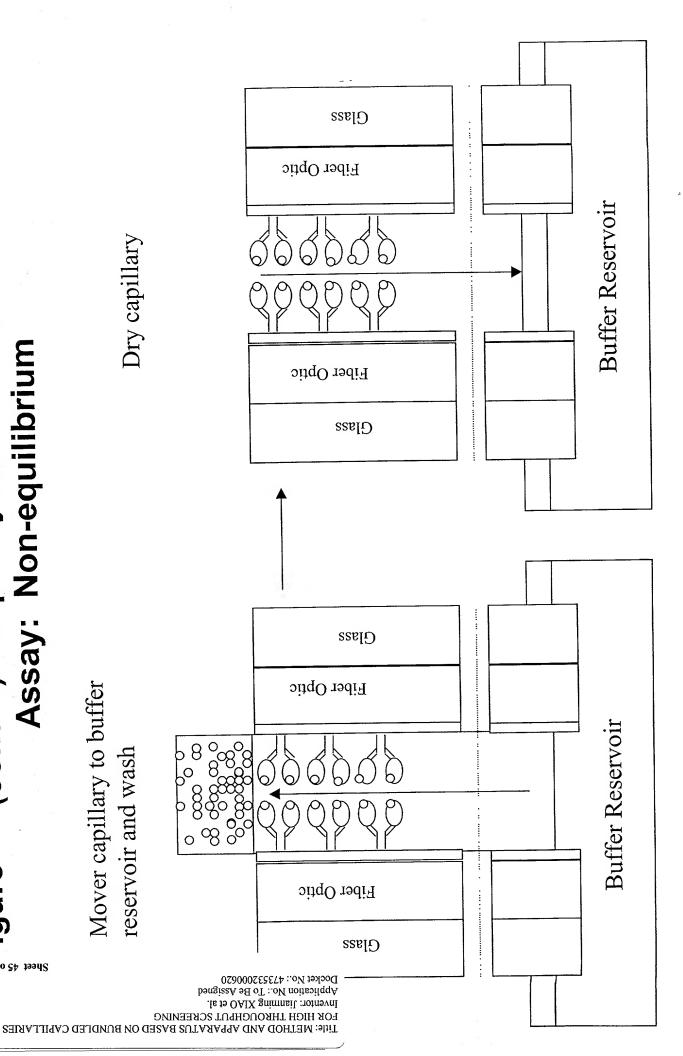


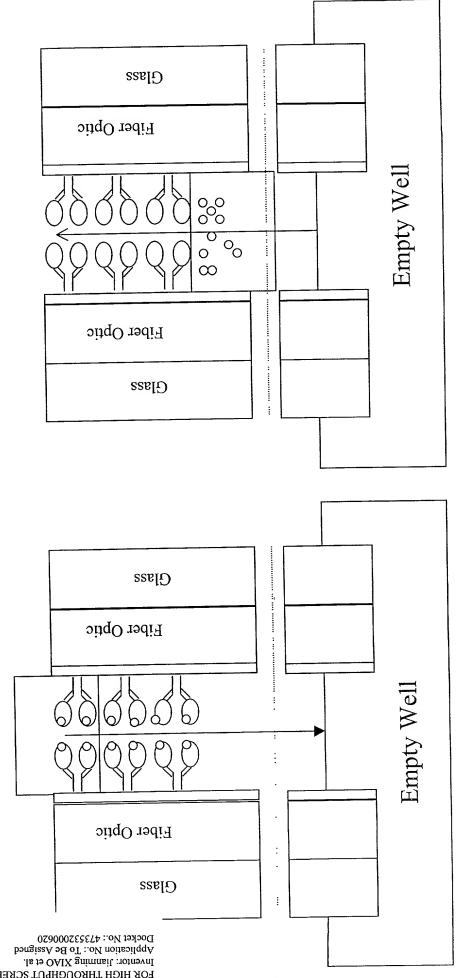
Figure 34 (cont. 4). Capillary Based Receptor Binding Assay: Non-equilibrium

Assay: Non-equility

Push an acid plug or detect

% bound using fiber optic

Apply vacuum after pug travels down capillary



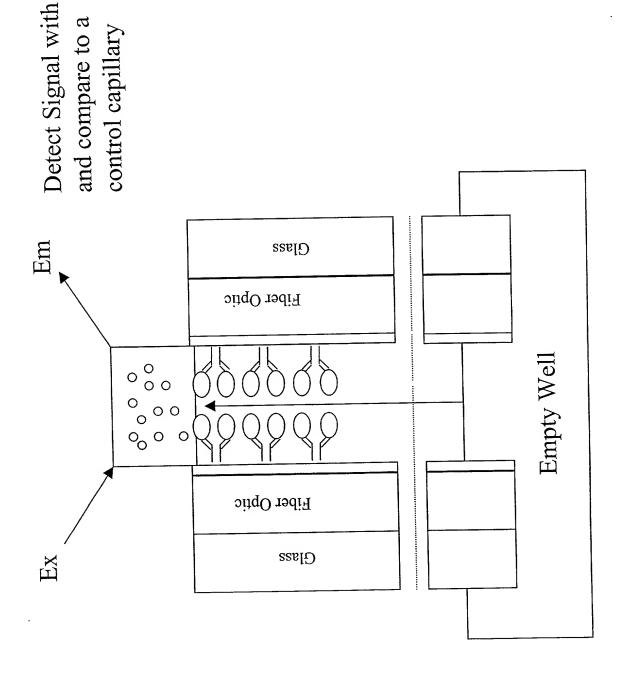
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based detection

Figure 34 (cont. 5). Capillary Based Receptor Binding

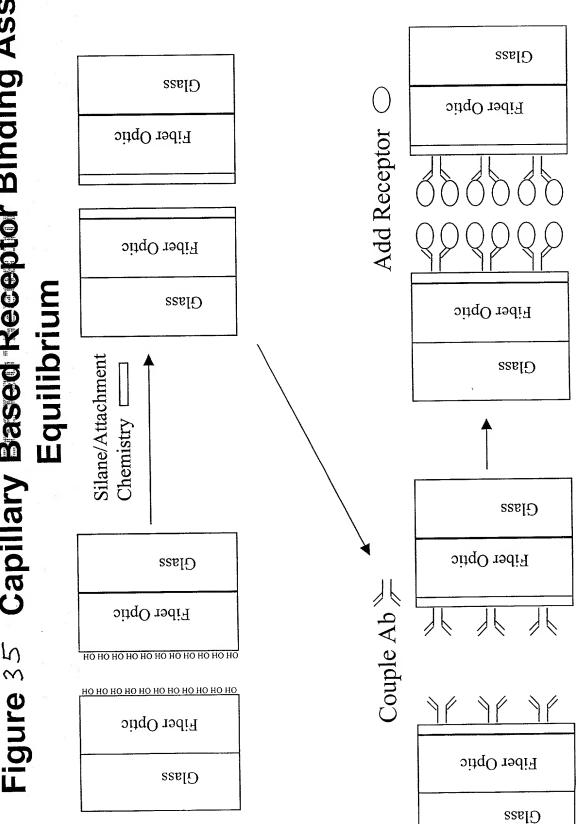
Assay: non-equilibrium



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Capillary Based Receptor Binding Assay: Figure 35



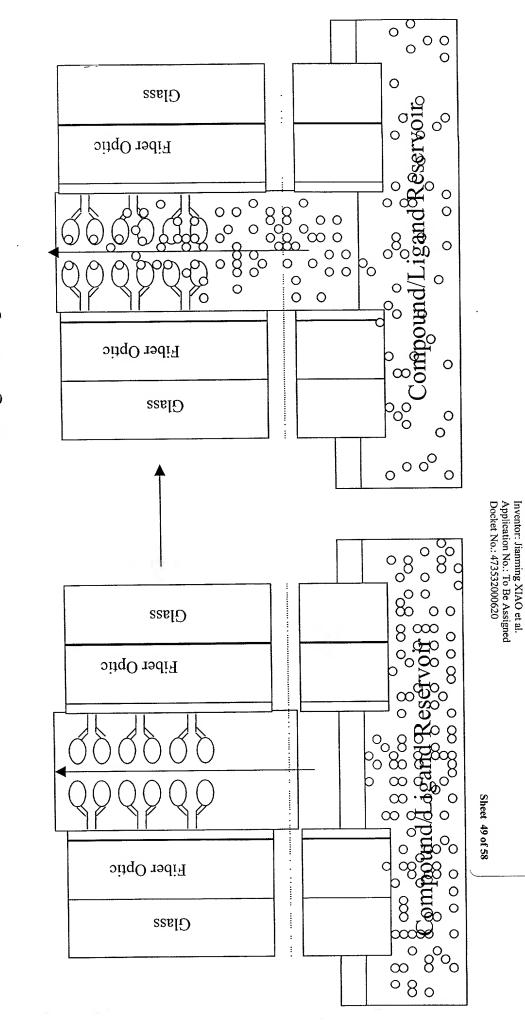
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Figure 35 (cont. 1). Capillary Based Receptor Binding Assay: Equilibrium

Move Capillary to compound/ligand reservoir.

Add solution and let system reach equilibrium. Detect equilibrium using fiber optic base detection.



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Figure 35 (cont. 2). Capillary Based Receptor Binding

Assay: Equilibrium

reservoir and wash capillary with buffer. Detect % bound using fiber optic based detection. Move capillary to a buffer Sheet 50 of 58

Dry Capillary

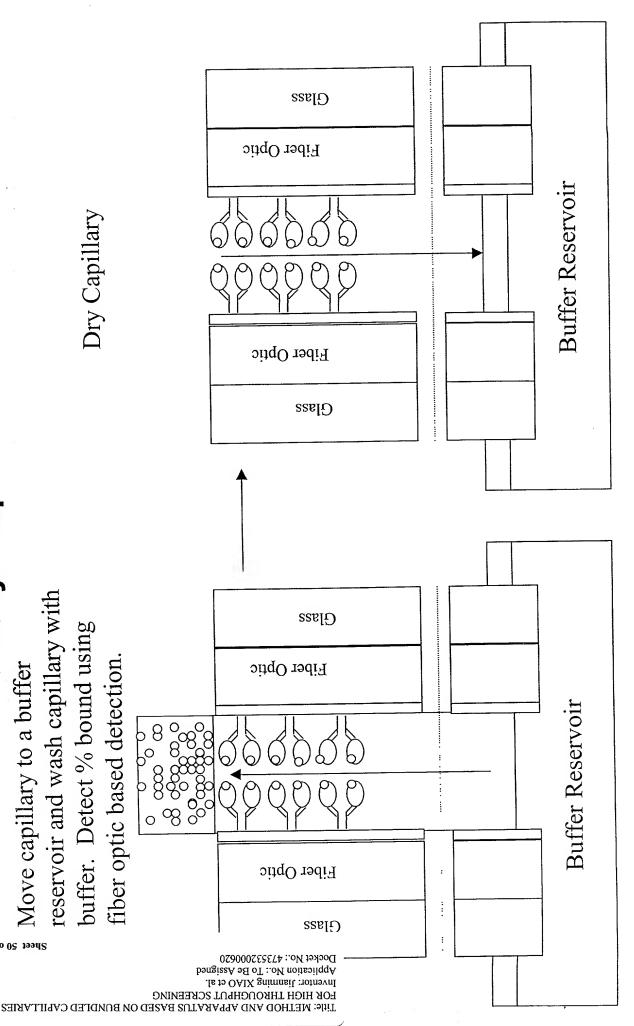


Figure 35 (cont. 3). Capillary Based Receptor Binding

Assay: Equilibrium

Detect signal using fiber optic base detection or elute bound ligand with acid.

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after pug travels down capillary Apply vacuum

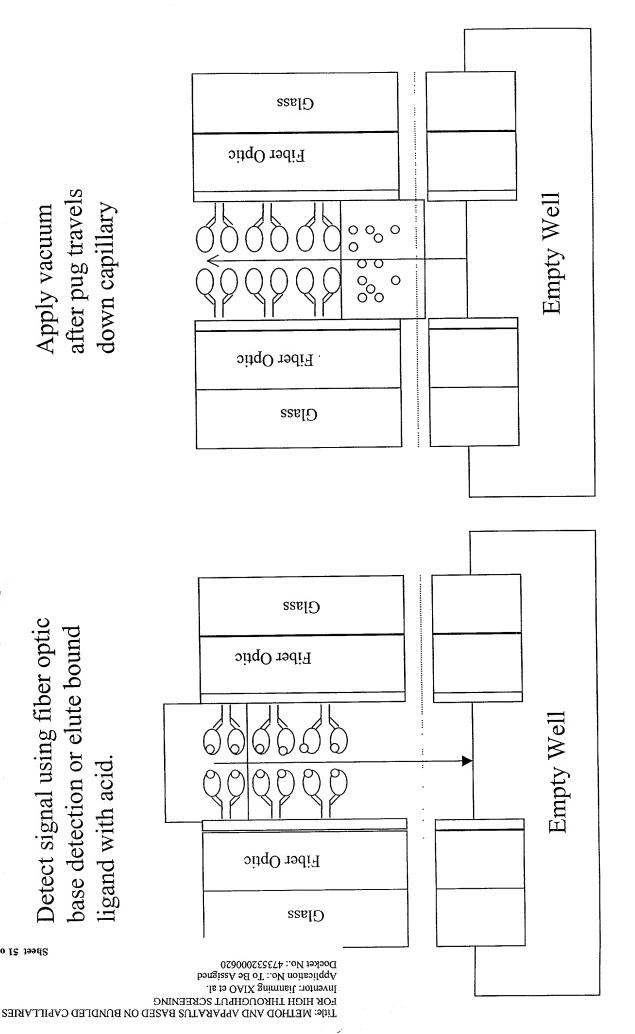
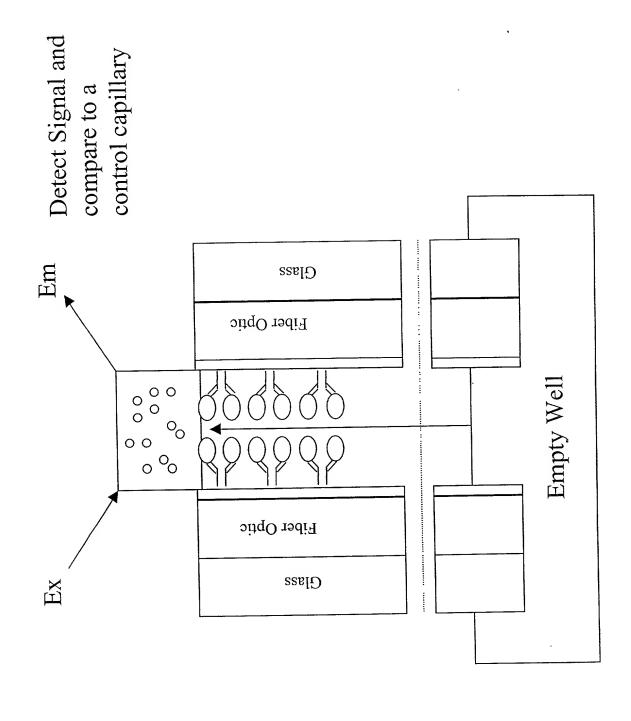


Figure 35 (cont. 4). Capillary Based Receptor Binding

Assay: Equilibrium



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Figure 36

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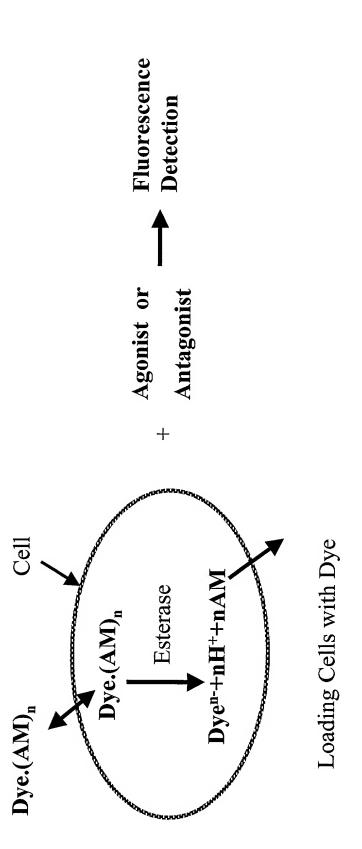


Figure 37

Assay Based on Tracking Cytosolic [Ca++]

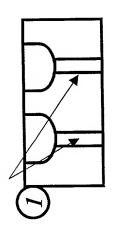
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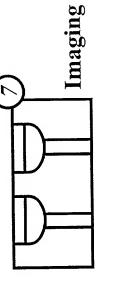
Protein Array & Cell Array

Library of antigen or antibody

Attached to magnetic beads

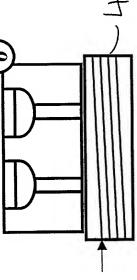


Aspiration from top



De-magnetize

Mixing circle



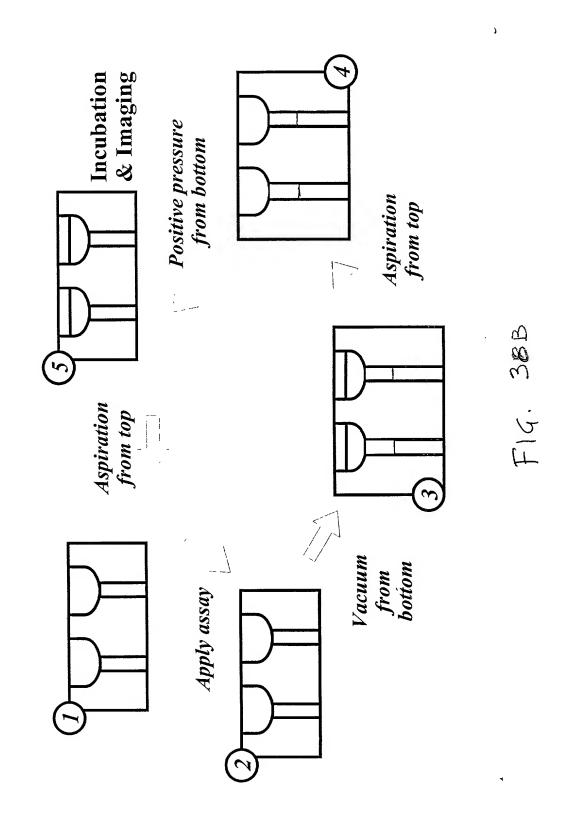
Magnetize & Washing circle

Seal Seal

Binding interaction

F19. 38A

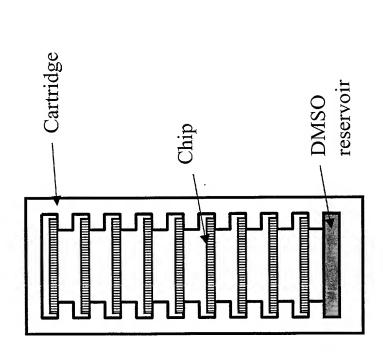
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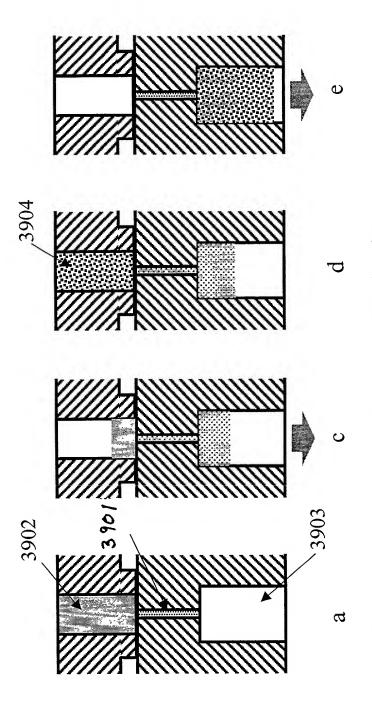
Fig. 39 One embodiment of the capillary array cartridge design



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Fig. ψ_0 Metering with through hole plates and mixing



3901 - compound and compound storage chamber

3902 - reagent A (i.e. enzyme) in through hole plate A

3903 - mixing/reaction chamber

04 – reagent B (i.e. substrate) in through hole plate B

82 lo 82 199d2

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